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| 09/498,098      | 02/04/2000  | Jeffrey Stack        | AURO1330            | 8316             |

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EXAMINER

ANGELL, JON E

ART UNIT PAPER NUMBER

1635

DATE MAILED: 08/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/498,098

Applicant(s)

STACK ET AL.

Examiner

Jon Eric Angell

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 May 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9, 11-38, 40, 50, 55, 60 and 80-87 is/are pending in the application.
- 4a) Of the above claim(s) 55 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 50 is/are allowed.
- 6) ☒ Claim(s) 1-9, 11-38, 40 and 80-87 is/are rejected.
- 7) ☒ Claim(s) 60 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 20 October 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 5/24/04.
- ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: \_\_\_\_\_.

### **DETAILED ACTION**

This Action is in response to the communication filed on 5/24/04. The amendment has been entered. Claims 1-9, 11-38, 40, 50, 55, 60 and 80-87 are currently pending in the application and are addressed herein.

Applicant's arguments are addressed on a per section basis. The text of those sections of Title 35, U.S. Code not included in this Action can be found in a prior Office Action. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's arguments.

Claim 55 has been withdrawn from consideration in a previous Office Action for the reasons of record. Claims 1-9, 11-38, 40, 50, 60 and 80-87 are examined herein.

### ***Information Disclosure Statement***

The information disclosure statement (IDS) submitted on 5/24/04 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9 and 11-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not

described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This is a new matter rejection.

It is noted that claim 1 has been amended such that lines 12-16 of the claims now reads, “cleavage of said linker moiety by said protease activity decreases the coupling of said destabilization domain to said reporter moiety thereby decreasing the stability of said reporter moiety...” The instant claim is based on the amendment that now indicates that cleaving the linker moiety decreases the coupling of the destabilization domain to the reporter thereby decreasing stability of the reporter. Since the rejection is necessitated by the amendment, this Action is Final.

The instant claims are drawn to a method of detecting a protease activity in a cell comprising: a) i), ii) and iii) as indicated in the claim; wherein said linker moiety comprises a protease cleavage site for said protease activity and cleavage of said linker moiety by said protease activity decreases the coupling of said destabilization domain to said reporter moiety thereby decreasing the stability of said reporter moiety, and... b) as indicated in claim 1.

The instant claim now indicates that when the destabilization domain is separated from the reporter domain, via cleavage of the linker moiety, there is a decrease in stability of the reporter moiety.

It is noted that the specification indicates that the destabilization domain destabilizes the reporter moiety when the destabilization domain is coupled to the reporter. Since cleavage of the linker moiety with a protease would dissociate the destabilization domain from the moiety domain, the result would not be a decrease in the stability of the reporter moiety, but rather an

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increase in the stability of the reporter moiety. That is, since the destabilization domain (which destabilizes the reporter when they are together) is removed from the reporter moiety (by cleavage of the linker) the reporter moiety should have an increase in stability.

The specification, at the time of filing only disclosed that dissociating the destabilization domain and reporter moiety increases the stability of the reporter moiety. Since there is no support in the specification, at the time of filing, that indicates dissociating the destabilization domain from the reporter can decrease the stability of the reporter, the new claims is considered new matter. If applicants disagree, they are asked to indicate where in the specification support for the new claim can be found by indicating the precise page and line numbers where support can be found.

***Claim Rejections - 35 USC § 112, first paragraph***

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-9, 11-38, 40 and 80-87 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. For the reasons of record,

Additionally, claims 1-9, 11-38, 40 and 80-87 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, in view of the written description requirement indicated above, for the reasons of record.

Briefly, for convenience, the instant claims are drawn to a method of detecting a protease activity in a cell (claims 1-9, 11-22, 80, 83, 85-87), a method for increasing the concentration of one or more target proteins in a cell (claims 23-37, 81), as well as a method for destabilizing a target protein in a cell (claims 38, 40, 82, 84) wherein the methods utilize a molecule comprising a destabilization domain wherein the destabilization domain can be **a ubiquitin homolog** (see claims 6, 31, 38, etc.). The specification has not met the written description guidelines for the ubiquitin homologs encompassed by the claims, for the reasons of record. Furthermore, since the specification has not adequately described the ubiquitin homologs encompassed by the claims, one of skill in the art would not know how to make and use the claimed invention to the full scope encompassed by the claims without performing an undue amount of additional experimentation.

### ***Response to Arguments***

Applicant's arguments filed 5/24/04 have been fully considered but they are not persuasive.

Applicants argue that the definition of "homolog" on page 24, lines 8-13 of the specification would clearly indicate to one of skill in the art that the ubiquitin homologs of the invention would have the desired function of retaining ubiquitin function. Applicants assert that this definition in conjunction with the definition presented on pages 13-14 (discussed in the previous Office Action) satisfies the written description guidelines.

In response, Applicants arguments have been fully considered but are not persuasive. It is respectfully pointed out that the applicants are indicating in their response that the claims, as defined in the specification on pages 13-14 and 24, would clearly indicate to one of skill in the art that *any* ubiquitin homologue that had ubiquitin function is encompassed by the claims. The Examiner agrees with this assessment of what is encompassed by the term “homolog”. However, the disclosure only indicates what are “ubiquitin homologs” by function only, not by structure. That is, the claims encompass any ubiquitin homologue that has the same function as ubiquitin. However, the specification has not adequately described the structure of the ubiquitin homologs encompassed by the claims—the disclosure does not indicate any structure-function relationship such that one of skill in the art would recognize the ubiquitin homologs encompassed by the claims. Simply describing the homologs by their function does not adequately describe the homologs encompassed by the claims. As such, the claims remain rejected for the reasons of record.

With respect to the enablement rejection, applicants only argue that since the definition of homolog on pages 13-14 of the specification and the discussion regarding destabilization domains and the functionality thereof is sufficient to satisfy the written description and enablement requirements of 35 USC 112, first paragraph, and therefor, applicants contend, one of skill in the art would understand how to make and use the invention with ubiquitin homologs as destabilization domains. Since the applicants’ arguments regarding the written description rejection are not persuasive, neither are applicants’ arguments with respect to the enablement rejection. Therefore, the instant claims remain rejected under 35 USC 112, first paragraph for not being enabled for the full scope encompassed by the claims.

### *Claim Objections*

Claim 60 is objected to because of the following informalities: line 9 of claim 60 recites, "a-NH-ubiquitin protein". This appears to be typographical error which should read " $\alpha$ -NH ubiquitin protein". Appropriate correction is required.

### *Miscellaneous*

The rejection of claims under 35 USC 112, second paragraph have been withdrawn in view of the amendment to the claims.

The rejection of claims under 35 USC 112, first paragraph that are not reiterated herein have been withdrawn in view of the claim amendments and/or applicants arguments.

### *Conclusion*

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,



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however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.


This application contains claim 55, drawn to an invention nonelected with traverse. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon Eric Angell whose telephone number is 571-272-0756. The examiner can normally be reached on Mon-Fri, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on 571-272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Art Unit 1635



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